

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Withdrawn) A nucleic acid that encodes a chimeric transcription factor comprising:

(a) an inducible activation domain responsive to signal transduction from an extracellular ligand; and

(b) a synthetic DNA binding domain that binds a nucleic acid sequence and activates transcription of an endogenous gene

wherein the activation domain is operably linked to the DNA binding domain such that activity of the transcription factor can be regulated.

2. (Withdrawn) The nucleic acid of claim 1 wherein the activation domain is responsive to a signal transduction pathway selected from the group consisting of Jak-STAT, MAP kinases, phosphatidyl inositol /Ca⁺⁺, and cyclic nucleotides.

3. (Withdrawn) The nucleic acid of claim 1 wherein the activation domain is the ligand binding domain of an intracellular receptor.

4. (Withdrawn) The nucleic acid of claim 1 wherein the synthetic DNA binding domain contains at least one non-zinc finger polypeptide.

5. (Withdrawn) The nucleic acid of claim 1 wherein the synthetic DNA binding domain contains at least one modified zinc finger.

6. (Withdrawn) The nucleic acid of claim 5 wherein the synthetic DNA binding domain binds to a DNA sequence within about 2,000 base pairs of the transcription unit.

7. (Withdrawn) The nucleic acid of claim 5 wherein the synthetic DNA binding domain binds to a unique 9 base pair sequence within about 2,000 base pairs of the transcription unit.

8. (Withdrawn) The nucleic acid of claim 5 wherein the synthetic DNA binding domain binds to a sequence within the gene.

9. (Withdrawn) The nucleic acid of claim 1 wherein the activation domain is responsive to a Cytokine receptor signal transduction pathway and the synthetic DNA binding domain contains at least 1 modified zinc finger.

10. (Withdrawn) The nucleic acid of claim 1 wherein the activation domain is responsive to a Growth Factor signal transduction pathway and the synthetic DNA binding domain contains at least 1 modified zinc finger.

11. (Withdrawn) The nucleic acid of claim 1 wherein the activation domain is responsive to a G-protein coupled receptor signal transduction pathway and the synthetic DNA binding domain contains at least 1 modified zinc finger.

12. (Withdrawn) The nucleic acid of claim 1 wherein the activation domain is the ligand binding domain of an intracellular receptor and the synthetic DNA binding domain contains at least 1 modified zinc finger.

13. (Withdrawn) An expression vector comprising a nucleic acid selected from the group consisting of:

- (a) claim 1
- (b) claim 2
- (c) claim 3

- (d) claim 4
- (e) claim 5
- (f) claim 6
- (g) claim 7
- (h) claim 8
- (i) claim 9
- (j) claim 10
- (k) claim 11; and
- (l) claim 12.

- 14. (Withdrawn) A cell containing an expression vector of claim 13.
- 15. (Withdrawn) The cell of claim 14 wherein the cell is of mammalian origin.
- 16. (Withdrawn) The cell of claim 15 wherein the cell is of human origin.
- 17. (Withdrawn) The cell of claim 14 wherein the cell is a bacterial cell.
- 18. (Withdrawn) The cell of claim 14 wherein the cell is a yeast cell.
- 19. (Withdrawn) The cell of claim 14 wherein the cell is an insect cell.
- 20. (Withdrawn) The cell of claim 14 wherein the cell is a plant cell.
- 21. (Withdrawn) A process for expression of a chimeric transcription factor in a recombinant host cell, comprising:
 - (a) transferring the expression vector of Claim 13 into suitable host cells; and
 - (b) culturing the host cells under conditions that allow expression of the chimeric transcription factor from the expression vector.
- 22. (Withdrawn) The process of claim 21 further comprising
 - (c) isolating the transcription factor from the cell.

23. (Withdrawn) A polypeptide comprising a chimeric transcription factor isolated by the process of claim 22.

24. (Withdrawn) A monospecific antibody that immunologically reacts to the chimeric transcription factor of claim 23.

25. (Withdrawn) A cell comprising the polypeptide of claim 23

26. (Withdrawn) The cell of claim 25 wherein the polypeptide is introduced by liposome, electroporation, microinjection, micro-ballistic projectile, or polypeptide mediated transduction.

27. (Withdrawn) A method comprising the steps:
a) contacting a compound with a cell of claim 14 wherein the cell expresses a chimeric transcription factor;
b) measuring expression of a gene under promotional control of said transcription factor;
c) determining the effect of the compound on the amount of gene expression.

28. (Withdrawn) The method of claim 27 wherein the cell is modified to modulate the repressed state of the endogenous gene.

29. (Withdrawn) The method of claim 28 wherein the cell is modified by pre-exposure to drugs selected from a group consisting of: trichostatin A (TSA), and 5-aza-2'deoxyctidine (5-Aza-dC).

30. (Withdrawn) The method of claim 27 wherein step (b) measures the level of mRNA of the endogenous gene.

31. (Withdrawn) The method of claim 27 wherein step (b) measures the level of protein produced by the endogenous gene.

32. (Withdrawn) The method of claim 27 wherein the endogenous gene is an enzyme and step (b) is measured by monitoring the amount of enzyme activity of the endogenous gene.

33. (Withdrawn) The method of claim 33 wherein the endogenous gene is an enzyme selected from the group consisting of alkaline phosphatase, myeloperoxidase, and a serine protease.

34. (Withdrawn) The method of claim 27 wherein the induced endogenous gene produces a cell surface protein.

35. (Withdrawn) The method of claim 34 wherein the cells surface protein is selected from the group consisting of a CD antigen, a non-CD antigen transmembrane protein, and placental alkaline phosphatase.

36. (Withdrawn) The method of claim 27 wherein the cells are lysed and the product of the induction of the endogenous gene is measured in the cell lysate.

37. (Withdrawn) The method of claim 27 wherein the induction of the endogenous gene results in a change in cellular phenotype that is measured in step (b).

38. (Withdrawn) The method of claim 37 wherein the cellular phenotype is translocation of a protein from one cellular component to a different cellular component.

39. (Withdrawn) A method comprising the steps:
a) contacting a compound, an extracellular ligand and a cell of claim 14, said cell being capable of responding to said ligand and containing a chimeric transcription factor;

b) measuring expression of an endogenous gene under transcription control of said exogenous transcription factor; and

c) determining the effect of the compound on the amount of gene expression.

40. (Withdrawn) The method of claim 39 wherein the cell is modified to modulate the repressed state of the endogenous gene.

41. (Withdrawn) The method of claim 40 wherein the cell is modified by pre-exposure to drugs selected from a group consisting of: trichostatin A (TSA), and 5-aza-2'deoxyctidine (5-Aza-dC).

42. (Withdrawn) The method of claim 39 wherein step (b) measures the level of mRNA of the endogenous gene.

43. (Withdrawn) The method of claim 39 wherein step (b) measures the level of protein produced by the endogenous gene.

44. (Withdrawn) The method of claim 39 wherein the endogenous gene is an enzyme and step (b) is measured by monitoring the amount of enzyme activity of the endogenous gene.

45. (Withdrawn) The method of claim 44 wherein the endogenous gene is an enzyme selected from the group consisting of alkaline phosphatase, myeloperoxidase, and a serine protease.

46. (Withdrawn) The method of claim 39 wherein the induced endogenous gene produces a cell surface protein.

47. (Withdrawn) The method of claim 46 wherein the cells surface protein is selected from the group consisting of a CD antigen, a non-CD antigen transmembrane protein, and placental alkaline phosphatase.

48. (Withdrawn) The method of claim 39 wherein the cells are lysed and the product of the induction of the endogenous gene is measured in the cell lysate.

49. (Withdrawn) The method of claim 39 wherein the induction of the endogenous gene results in a change in cellular phenotype that is measured in step (b).

50. (Withdrawn) The method of claim 49 wherein the cellular phenotype is translocation of a protein from one cellular component to a different cellular component.

51. (Withdrawn) A nucleic acid that encodes a chimeric transcription factor comprising:

(a) an inducible activation domain responsive to signal transduction from an extracellular ligand; and

(b) a synthetic DNA binding domain that binds to a nucleic acid sequence and activates transcription of an endogenous receptor gene wherein the activation domain is operably linked to the DNA binding domain such that activity of the transcription factor can be regulated.

52. (Withdrawn) An expression vector comprising a nucleic acid of claim 51.

53. (Withdrawn) A cell containing the expression vector of claim 52.

54. (Withdrawn) The cell of claim 53 wherein the cell is of mammalian origin.

55. (Withdrawn) The cell of claim 54 wherein the cell is of human origin.

56. (Withdrawn) The cell of claim 53 wherein the cell is a bacterial cell.

57. (Withdrawn) The cell of claim 53 wherein the cell is a yeast cell.

58. (Withdrawn) The cell of claim 53 wherein the cell is an insect cell.
59. (Withdrawn) The cell of claim 53 wherein the cell is a plant cell.
60. (Withdrawn) A process for expression of a chimeric transcription factor in a recombinant host cell, comprising:
- (a) transferring the expression vector of Claim 52 into suitable host cells;
- and
- (b) culturing the host cells under conditions that allow expression of the chimeric transcription factor from the expression vector.
61. (Withdrawn) The process of claim 60 further comprising
- (c) isolating the transcription factor from the cell.
62. (Withdrawn) A polypeptide comprising a chimeric transcription factor isolated by the process of claim 61.
63. (Withdrawn) A cell wherein the polypeptide of claim 62 is introduced by nonrecombinant means..
64. (Withdrawn) The cell of claim 63 wherein the polypeptide is introduced by liposome, electroporation, microinjection, micro-ballistic projectile, or polypeptide mediated transduction
65. (Withdrawn) A monospecific antibody that immunologically reacts to the chimeric transcription factor of claim 62.
66. (Withdrawn) A method to modulate the amount of a receptor comprising the steps:
- a) providing a cell of claim 53 wherein the cell contains an inducible transcription factor that up-regulates a receptor of interest in the cell; and
 - b) stimulating the function of the transcription factor with an extracellular ligand such that the receptor is produced by the cell

wherein the amount the receptor is modulated by the activity of the transcription factor.

67. (Withdrawn) A method comprising the steps:
- a) contacting a compound with an un-stimulated cell of claim 53 and contacting a compound with a stimulated cell of claim 53 such that the stimulated cell expresses a receptor;
 - b) measuring the activity of the receptor in the un-stimulated cell and the stimulated cell; and
 - c) determining the effect of the compound on the activity of the receptor.
68. (Withdrawn) A method comprising the steps:
- a) contacting a compound and an extracellular ligand with an unstimulated cell of claim 53 and contacting a compound and an extracellular ligand with a stimulated cell of claim 53 such that the stimulated cell expresses a receptor;
 - b) measuring the activity of the receptor in the unstimulated cell and the stimulated cell; and
 - c) determining the effect of the compound on the activity of the receptor.
69. (Withdrawn) A nucleic acid that encodes a chimeric transcription factor comprising:
- a) a constitutively active domain;
 - b) a synthetic DNA binding domain that binds to a nucleic acid sequence and activates transcription of an endogenous gene; and
 - c) a membrane anchoring domain that contains a protease cleavage site
- wherein the constitutively active domain is operably linked to the DNA binding domain such that the transcription factor is active in an unregulated fashion.

70. (Withdrawn) An expression vector containing the nucleic acid of claim 69.

71. (Withdrawn) A cell that contains the expression vector of claim 70.

72. (Withdrawn) A method comprising the steps:

- a) contacting a compound with a cell of claim 71, said cell containing a membrane bound, constitutively active transcription factor;
- b) stimulating activity of a protease by the compound to release the transcription factor from the membrane and therefore allowing the transcription factor to translocate to the nucleus;
- c) measuring expression of a gene under promotional control of the membrane bound transcription factor; and
- d) determining the effect of the compound on the amount of gene expression.

73. (Withdrawn) A method comprising the steps:

- a) contacting a compound and an extracellular ligand with a cell of claim 71, said cell containing a membrane bound, constitutively active transcription factor;
- b) stimulating activity of a protease by either the compound or the ligand to release the transcription factor from the membrane and therefore allowing the transcription factor to translocate to the nucleus;
- c) measuring expression of a gene under promotional control of the membrane bound transcription factor; and
- d) determining the effect of the compound on the amount of gene expression.

74. (Withdrawn) A compound discovered using the method of claim 27.

75. (Withdrawn) A pharmaceutical composition comprising a compound of claim 74.

76. (Withdrawn) A compound discovered using the method of claim 39.
77. (Withdrawn) A pharmaceutical composition comprising a compound of claim 76.
78. (Withdrawn) A compound discovered using the method of claim 67.
79. (Withdrawn) A pharmaceutical composition comprising a compound of claim 78.
80. (Withdrawn) A compound discovered using the method of claim 68.
81. (Withdrawn) A pharmaceutical composition comprising a compound of claim 81.
82. (Presently Amended) A ~~transcription factor regulator~~ compound that modulates the response of an extracellular ligand identified by a method comprising the steps of:
- a) contacting a compound suspected of being a ~~transcription factor regulator~~ compound that modulates the response of an extracellular ligand with a cell having a nucleus and containing a membrane-bound, constitutively active transcription factor produced by expression of a nucleic acid construct comprising an expression vector containing:
- i) a constitutively active domain;
- ii) a synthetic DNA binding domain that binds to a nucleic acid sequence and activates transcription of an endogenous gene; and

iii) a membrane anchoring domain that contains a protease cleavage site, wherein the constitutively active domain is operably linked to the DNA binding domain such that the transcription factor is active in an unregulated fashion;

b) stimulating activity of a protease by the compound to release the transcription factor from the membrane, thereby allowing the transcription factor to translocate to the nucleus; and

c) measuring expression of a gene under promotional control of the membrane-bound transcription factor, whereby an increase or decrease in expression of the gene is indicative that the compound ~~is a transcription factor regulator~~ modulates the response of an extracellular ligand.

83. (Presently Amended) A pharmaceutical composition comprising a ~~transcription factor regulator compound~~ of claim 82.

84. (Presently Amended) A ~~transcription factor regulator compound that~~ modulates the response of an extracellular ligand identified by a method comprising the steps of:

a) contacting a compound suspected of being a ~~transcription factor regulator compound~~ that modulates the response of an extracellular ligand with an extracellular ligand and a cell having a nucleus and containing a membrane-bound, constitutively active transcription factor produced by

expression of a nucleic acid construct comprising an expression vector
containing:

- i) a constitutively active domain;
- ii) a synthetic DNA binding domain that binds to a nucleic acid
sequence and activates transcription of an endogenous gene;

and

- iii) a membrane anchoring domain that contains a protease
cleavage site, wherein the constitutively active domain is
operably linked to the DNA binding domain such that the
transcription factor is active in an unregulated fashion;

b) stimulating activity of a protease by either the compound or the
ligand to release the transcription factor from the membrane, thereby allowing
the transcription factor to translocate to the nucleus; and

c) measuring expression of a gene under promotional control of the
membrane-bound transcription factor, whereby an increase or decrease in
expression of the gene is indicative that the compound ~~is a transcription factor~~
~~regulator~~ modulates the response of an extracellular ligand.

85. (Presently Amended) A pharmaceutical composition comprising a
~~transcription factor regulator~~ compound of claim 84.